Correspondence

Human Growth Hormone—Orphan With a Silver Spoon

To THE EDITOR: Douglas Frasier, a fellow pediatric endocrinologist, indicated that it was inappropriate to consider recombinant human growth hormone as a privileged "orphan" drug under the Orphan Drug Act because that allowed its exclusive producers, Genentech and Eli Lilly, to reap excessive profits.[1] Including this drug in the special orphan category was defended by representatives of Genentech and the Food and Drug Administration (FDA), successfully in my opinion. I agree that the availability of recombinant human growth hormone has proved beneficial and even life-saving in children with growth hormone deficiency. Not only does it prevent dwarfism, but it normalizes facial features and body configuration and prevents the severe hypoglycemia that can lead to brain damage. In view of the limited number of children with hypothalamic or hypopituitary growth deficiency, I think pharmaceutical companies deserve a good return for developing this product.

On the other hand, I am disturbed by efforts to push the use of recombinant growth hormone in children without growth hormone deficiency, including normal, healthy children with short stature and girls with Turner's syndrome. The potential financial bonanza here would make the $200 million profit estimates by Frasier appear to be small change.

We know the effects of excess growth hormone in humans with pituitary gigantism and acromegaly. Not only is height increment accelerated, but coarse thick features appear, there is enlargement of the hands and feet, and diabetes mellitus develops. Growth hormone in vitro increases the growth rate of many cells, raising the specter of neoplasia. Although the recent cases of leukemia in growth-hormone-treated children in Japan were not proved to be due to this treatment,[2] there is still cause for concern, in my mind, particularly in children with Turner's syndrome who have a chromosomal defect.

Genentech has made efforts to ensure the ethical use of its product by distributing it through pediatric endocrinologists. Recombinant human growth hormone is approved by the FDA only for use in growth hormone deficiency. There is now an application for FDA approval for its use in treating Turner's syndrome, however. There is pressure for its use in normal, short children from parents who have been led to think of it as a "height hormone" instead of a substance affecting many cells and metabolic systems.

Lately we have seen evidence here in northern California, the home of Genentech, that marketing people are beginning to prevail over the ethical medical scientists who previously were apparently in control. Pediatricians have been paid honoraria to attend free dinners in San Francisco to hear talks on growth hormone. The largest children's hospital in northern California had a "free growth screening day." Although the above events were sponsored by Genentech, the announcement gave no hint that Genentech was involved. A local Genentech representative mentioned that his income was linked to the amount of growth hormone prescribed in his territory. This same representative was involved in a "height screening program" in public schools in which the parents of short children were advised to see a physician concerning their child's height. A recent private newsletter mailed to all pediatric endocrinologists reported highlights of pediatric research meetings and clearly emphasized the viewpoints of Genentech investigators; the issue was produced by funding from Genentech.[3]

It could be argued that the above activities are simply aggressive marketing aimed at discovering undiagnosed growth hormone deficiency. In my mind, however, these activities are ethically questionable; they represent attempts to expand the use of growth hormone to persons without hormone deficiency and are inappropriate for a privileged orphan drug. In addition, I feel that the manufacturers should be required to show evidence that they are taking measures to prevent recombinant growth hormone from reaching the black market, where the drug is already being abused by athletes and others who can afford the high cost.

The opportunity for growth hormone to become a financial superstar lies in its use in short children without proved growth hormone deficiency (particularly in healthy short children), where its efficacy and long-term safety have not been shown. It is here that we can expect the most pressure to prescribe it, and there is disturbing evidence that few holds will be barred in attempting to reap the immense potential profits. Caveat emptor, FDA.

EDGAR J. SCHOEN, MD
Department of Pediatrics
Kaiser Permanente Medical Center
280 W MacArthur Blvd
Oakland, CA 94611-5693

REFERENCES

1. Frasier SD: Human growth hormone is not an orphan (Letter). N Engl J Med 1989; 321:1124-1125
2. Fisher DA, Job JC, Preece M, et al: Leukaemia in patients treated with growth hormone (Letter). Lancet 1988; 1:1159-1160
3. Clin Courier 1989 Oct; 7:1-11

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Dr Sherman Responds

To THE EDITOR: I welcome the opportunity to respond to Dr Schoen's recent comments about the use of human growth hormone.

Genentech's Protropin (somatrem for injection) is currently indicated for the treatment of short stature associated with growth hormone inadequacy in children. Our commitment to the appropriate use of growth hormone replacement therapy extends to our continuing efforts at monitoring its use in clinical practice. Of the estimated 12,000 patients in the United States currently receiving the therapy, more than half are enrolled and followed in a Genentech-sponsored postmarketing study. The National Cooperative Growth Study was designed, among other things, to disclose unexpected adverse effects of growth hormone treatment. We have now accumulated almost five years of safety- and efficacy-related information in children treated with growth hormone. Treatment-related side effects are rare, and physical changes related to growth hormone excess in children treated with somatrem are essentially unheard of.

In addition, Genentech has in place a very reliable, controlled distribution system for somatrem. This unique distribution system was voluntarily put into place by Genentech, and we think it efficiently mitigates against misuse of the hormone.

Dr Schoen accepts growth hormone for the treatment of children with growth hormone insufficiency but questions its evaluation in other groups of children whose growth is retarded. When only pituitary growth hormone was availa-

ble, its limited supply effectively precluded its use or study beyond the treatment of only the most severely growth hormone-deficient children.

One of the benefits of recombinant DNA methods is that the supply of growth hormone now allows us to carry out controlled studies in other disorders associated with severe short stature such as Turner's syndrome or chronic renal insufficiency. We at Genentech believe that it is our responsibility to support research that may lead to treatments of medical conditions or diseases beyond the initial indication for growth hormone inadequacy. This research, in conjunction with the good judgment of prescribing pediatricians, may lead to improved quality of life for children afflicted with a variety of diseases.

Genentech also feels that it is important to develop educational programs that will bring the availability of therapy for all patients who need it. Increasing parent awareness of the existence of growth disorders could include height screening programs. As Dr Schoen accurately points out, the result of a height screening program may be a recommendation to parents of extremely short children to see a physician concerning their child's height. While some of these children may be diagnosed as having insufficient growth hormone secretion, others have been found to have a variety of medical disorders requiring attention and treatment.

Genentech takes pride in its innovative laboratory and clinical science, product development, and educational programs. We remain committed to bringing the best of biomedical science to patients who can benefit from our products and will continue to take steps to ensure the ethical use of growth hormone.

BARRY SHERMAN, MD
Vice President, Medical Affairs
Genentech, Inc
460 Point San Bruno Blvd
South San Francisco, CA 94080

A Profile of California's Physician Assistants

To the Editor: Most of the 1,782 physician assistants (PAs) currently licensed to practice in California are graduates of the four in-state training programs begun in the early 1970s at Charles R. Drew School, University of Medicine and Science; Stanford University Medical Center; the University of Southern California; and the University of California at Davis.* In 1988 these programs collaborated in surveying their 1,263 graduates, using a mailed questionnaire, with telephone follow-up on a sample of initial nonrespondents. With data obtained from a majority of the graduates (641), the survey provides a reasonably representative profile of the backgrounds and the current roles of physician assistants in California health care.

About Their Backgrounds

The physician assistants surveyed had graduated between 1973 and 1987. Their ages in 1988 ranged from 25 to 63, with a median of 38. Over half (57%) were women. Most (58%) had entered training with a baccalaureate or higher degree. Clinical backgrounds varied, including nurses (30%), allied health (17%), corpsmen (16%), health aides (16%), and EMT/paramedics (9%). Nearly a third (30%) were of ethnic minority background, including 12% Hispanic, 11% African American, 3% Asian, 1% Native American, and 4% other. Most reported using a language other than English—usually Spanish—with their patients, and, notably, 34% of the total reported speaking Spanish with fluency.

Where They Practice

Most of the surveyed graduates are practicing in California (83%), with physician supervisors in primary care specialties (73%). Most work primarily in private physicians' offices (56%), with 14% in community clinics and 13% in county systems. Only 4% work primarily in urgent care or emergency departments, with 17% indicating hospital inpatient responsibilities. Almost half (45%) have more than one practice site, although most (87%) spend more than 70% of their time at their main site. Respondents reported having worked a mean of 3.7 years at their present main site, with an average current work week of 36.5 hours; 33% work more than 40 hours a week; 82% work more than 30 hours a week.

Types of Patients

The questionnaire asked for an estimate of the proportion of several types of patients seen in the respondent's "most recent week of regular practice." Estimated practice proportions exceeding 15% are interpreted here to indicate substantial involvement with a given category of patients. Using this measurement, 32% reported more than 15% of their practice involved patients not fluent in English, 61% reported more than 15% of their practice being with patients of ethnic minorities, 46% with patients on Medi-Cal, and 22% with patients whose care was unreimbursed. The same level of substantial involvement was reported for pa-

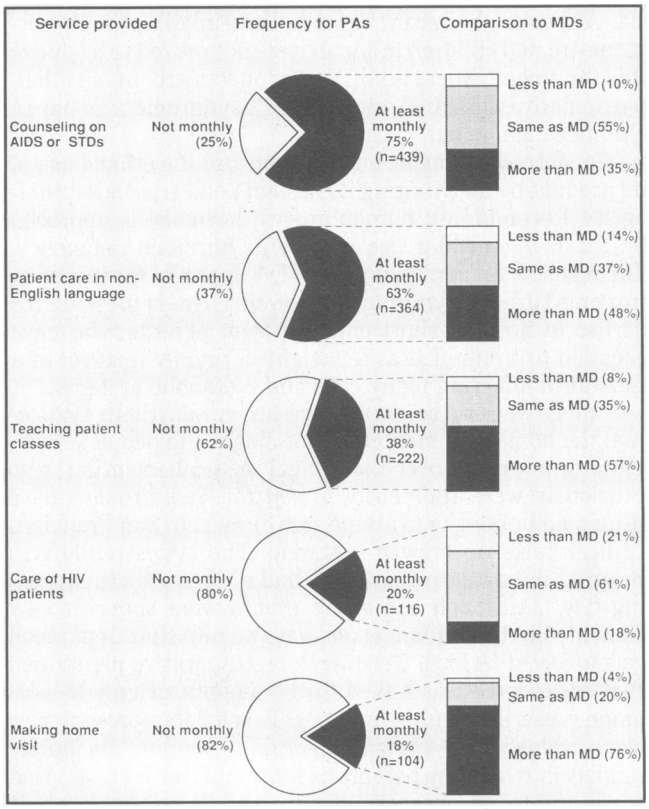

Figure 1.—Frequency of selected services provided at least monthly by physician assistants compared with their physician supervisors is shown.

*The work reported here represents a collaborative effort with Jack Liskin, PA, Director, USC/PA Program; Correne Treguboff, FNP, MHS (deceased), UC Davis FNP/PA Program; William Burnett, Principal Consultant, California Health Manpower Policy Commission; Wendell Wharton, PA, Director, Charles R. Drew Medex PA Program; Janet Mentink, FNP, MHS, Acting Director, UC Davis FNP/PA Program.